IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:			
Dane K. FISHER *et al.*		Art Unit:	1637
Appln. No.: 09/394,745		Examiner:	Young J. KIM
Filed:	September 15, 1999	Atty. Docket:	38-21(15454)B
For:	***Nucleic Acid Molecules and Other Molecules Associated with Plants***	Confirm. No.	4816

APPELLANT'S BRIEF

Commissioner for Patents
Washington, DC 20231

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-described patent application. A Notice of Appeal was filed on January 13, 2003. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter. *This Brief is submitted in triplicate.*

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant is unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 8-11 are pending. Claims 8-11 stand finally rejected under 35 U.S.C. §§ 101 and 112, first paragraph. Applicants appeal all of the rejections of claims 8-11.

4. Status of Amendments

Applicants have not filed any amendments subsequent to the Final Office Action mailed September 11, 2002 (Paper No. 14) ("Final Action"), in this case. Applicants filed a petition under 35 C.F.R. § 1.144 directed to the restriction requirement to select a single combination of nucleotide sequences for examination on January 10, 2003.

5. Summary of Invention

The invention is directed to a microarray comprising a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from a Markush group. *See* specification at pages 59, line 25 through page 62, line 7. The present invention is also directed to a microarray comprising nucleic acid molecules that are comprised of different sequences and at least about 250 nucleotide residues, wherein said nucleic acid molecules comprise nucleic acid sequences complementary to a single collection or combination of nucleotide sequences. *Id.*

6. Issues

The issues in this Appeal are:

(a) whether claims 8-11 are unpatentable under 35 U.S.C. § 101 for allegedly being unsupported by either specific and/or substantial utility or a well-established utility;

(b) whether claims 8-11 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because the claimed invention purportedly lacks utility; and

(c) whether claims 8-11 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged insufficiency of written description.

7. Grouping of Claims

The patentability of claims 8-11 is addressed together in Sections 8.A through 8.D below. A copy of the currently pending claims is attached hereto as Appendix A.

8. Argument

A. Summary of Appellant's Position

As the Supreme Court said in *Brenner v. Manson*, the "basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Applicants have met their part of the bargain – they have disclosed microarrays comprising nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, *e.g.,* the ability to efficiently analyze large amounts of nucleic acid molecules for a specific nucleotide sequence or sequences. This benefit is specific, not vague or unknown, and it is a "real world" or substantial benefit. Because the claimed microarrays comprise nucleic acid molecules that provide at least this benefit, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed microarrays for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Furthermore, Applicants have provided an adequate description of the claimed microarrays that demonstrates Applicants' possession of the claimed invention. The claimed microarrays comprise a genera of nucleic acid molecules wherein each genus of nucleic acid molecules, *i.e.*, the nucleic acid molecules comprising the nucleic acid sequences selected from the group consisting of SEQ ID NOs: 5776, 5781, 5782, 5783, 5785, 5787, 5800, 5804, 5815, 5818, etc., and their complements, has been described by the recitation of a common structural feature – the nucleotide sequences of SEQ ID NOs: 5776, 5781, 5782, 5783, 5785, 5787, 5800, 5804, 5815, 5818, etc., and their complements, respectively – which distinguishes molecules in the claimed genera from molecules not in the claimed genera. Because the specification demonstrates that Applicants had possession of (and have provided an adequate description of) the claimed microarrays comprising a genera of nucleic acid molecules, the specification satisfies the written description requirement of 35 U.S.C. § 112.

B. The Claimed Microarrays Have Legal Utility

Claims 8-11 were erroneously rejected under 35 U.S.C. § 101 as allegedly "not being supported by either specific and/or substantial utility or a well-established utility." Final Action at page 3. The Examiner acknowledges that the specification states that the claimed nucleic acid molecules are useful for studying genes that are agronomically significant, expression studies, and the detection of polymorphisms. *See, e.g.,* Office Action mailed March 18, 2002 (Paper Number 11), at page 6. However, the Final Action asserts that the claimed microarrays of the present invention fail "to have this substantial utility because the probes on the microarray, by their presence or absence, do not provide a real-world applicability to one of ordinary skill in the art." Final Action at page 4. Specifically, the Final Action asserts that "[t]he probes (which make up the microarray) as disclosed, do not provide to one of ordinary skill in the art, what their presence or the absence would be useful for." *Id.*

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson.* The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide <u>one</u> identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

The courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip*, 185 F.3d at 1366, 51 USPQ.2d at 1702. For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39

U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Applicants have asserted in the specification that the claimed microarrays provide identifiable benefits, for example, use for screening biological molecules and use as a highly efficient hybridization probe for expression profiling. *See, e.g.,* specification at page 42, line 11 through page 43, line 19; at page 59, line 25 through page 62, line 7; and the incorporated U.S. Patent No. 5,445,934 at column 10, lines 28-50. Either of these utilities described alone is enough to satisfy Section 101. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Microarrays Provide A Specific Benefit, *i.e.*, They Have Specific Utility

Applicants have asserted that the claimed microarrays comprising nucleic acid molecules[1] are themselves useful for the utilities disclosed in the specification, *e.g.*, use in screening for biological molecules, and as hybridization probes for expression profiling. Moreover, additional utilities for the claimed microarrays are disclosed by the specification and known to those of ordinary skill in the art, including screening for biological activity, determining relative binding affinity for a molecule bound to the a claimed microarray and creating a gradient of claimed nucleotide sequences in differing concentrations. *See, e.g.,* U.S. Patent No. 5,143,854 at column 2, lines 15-22; column 3, lines 22-61; column 8, lines 34-45; column 10, lines 32-53; and column 22, line 54 through column 23, line 12; and U.S. Patent No. 5,445,934 at column 10, lines 28-50 and column 22, lines 46-61 (incorporated by reference in their entireties, *see* specification at page

[1] It is irrelevant whether the corresponding mRNA or polypeptide have utility because Applicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed microarrays.

60, lines 17-19). Such screens are analogous to a cell-based assay, which has a legally sufficient utility.[2] Another utility disclosed in the specification includes use of the claimed microarrays to measure the level of mRNA in a sample.[3] *See* specification at page 42, line 26 through page 43, line 19; and at page 59, line 14 through page 60, line 6.

(a) Identifying Factors Involved in the Expression Response of a Cell, Tissue, or Plant

One of the utilities disclosed in the specification is to efficiently analyze large amounts of nucleic acid molecules for any of the nucleic acid molecules present on an embodiment of a claimed microarray to identify whether a sample (cell, tissue, plant, or other organism) has a mutation affecting the concentration of an mRNA or the pattern of expression encoded by one or more of the nucleic acid molecules present on the microarray. *See* specification at page 42, line 11 through page 43, line 19; at page 59, line 25 through page 62, line 7. Moreover, because one skilled in the art may design a microarray comprising a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from the Markush group, *see, e.g.,* claim 8, the claimed microarrays may be varied or customized to identify or screen for a particular nucleic acid molecule or molecules as designated by the designer. *See, e.g.,* Petition under 37 C.F.R. § 1.144, filed January 10, 2003, at pages 7-10. The Examiner argues that this utility, like many of the asserted utilities, is not specific or substantial, *see* Final Action at page 5, but does not provide

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[2] *See, e.g.*, MPEP § 2107 at page 2100-32.

[3] It is standard practice to screen populations of nucleic acids with EST sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, drought stress. Contrary to the Examiner's assertions, this is a use of the claimed nucleic acid molecules in a real world context.

any support (legal or factual) for the proposition that screening large populations of nucleic acids using the claimed microarrays is not a legal utility.

This particular disclosed utility is directly analogous to the utilities of a microscope, *i.e.*, the claimed microarrays may be used to locate and measure nucleic acid molecules within a sample, cell, or organism for a specific trait or traits as may be desired and designed by one skilled in the art. The Examiner denigrates this utility by asserting that this utility does not have "an immediately apparent benefit" because "[t]he artisan using the microarray of the Applicants would not know why the artisan should use the microarray of the claimed probes over other microarray comprising different probes that are isolated from plants (i.e. maize)." Final Action at page 5. However, the fact that, for example, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107 at page 2100-33.

Moreover, it is simply incorrect to state that an artisan using a claimed microarray would not know why the artisan should use the claimed microarray over other available microarrays. First, one of skill in the art, using the claimed microarrays has the ability to design a particular microarray tailored to the specifications required by the artisan himself. Secondly, because the claimed microarrays of the present invention are comprised of nucleic acid molecules isolated from various tissue of *Zea mays* (*e.g.*, ear tissue, pollen, kernel tissue, anther tissue, etc.) one skilled in the art would certainly know why the nucleic acid molecules of a claimed microarray are preferred to nucleic acid molecules or probes from other microarrays or other plants. *See. e.g.*, specification at page 91, line 5 through page 99, line 7 (Example 1).

Use of the claimed microarrays to analyze large quantities of nucleic acid molecules is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the

gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[4] Likewise, the claimed microarrays have utility even if the absence of particular nucleic acid molecules are detected in a sample. Indeed, the absence of a particular nucleic acid molecule or molecules usefully demonstrates that a sample, such as a plant or tissue, lacks a mutation that could alter the expression response of that particular sample.

The claimed microarrays have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, to determine whether a plant has a mutation affecting the concentration of mRNA or pattern of expression corresponding to any one or more of the nucleic acid molecules present on a claimed microarray. This benefit is immediately realized directly from the use of the claimed microarrays, not from the use of other microarrays. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Probes for Biological Molecules or As a Means to Assay for Relative Binding Efficiency

Other uses for the claimed microarrays are as probes for a multitude of biological molecules, such as nucleic acid homologues or transcription factors, or as a means to assay relative binding efficiency of such molecules. *See* specification at page 60, lines 14-16; the incorporated U.S. Patent No. 5,143,854 at column 2, lines 15-22; column 3, lines 22-61; column 8, lines 34-45; column 10, lines 32-53; and column 22, line 54 through column 23, line 12; and the incorporated U.S. Patent No. 5,445,934 at column 10, lines 28-50 and column 22, lines 46-61. The Examiner suggests that these uses are not legal utilities because "nucleic acid probes are not patented solely on their ability to hybridize to their complement," but rather the information gleaned from such hybridization. *See* Final Action at page 5. The Examiner's analysis is

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[4] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

incorrect and misstates the nature of the claimed invention. The specification discloses, for example, that the claimed microarrays can be used in real world applications such as those discussed above and additionally to isolate nucleic acid molecules of plants and organisms such as alfalfa, *Arabidopsis*, barley, *Brassica*, cotton, sunflower, *Phaseolus*, etc.[5] *See* specification at page 21, lines 11-17 and page 59, line 25 through page 60, line 6. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and thus has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

An illustrative example of a molecule that can be isolated using the claimed microarrays is a complement of a nucleic acid molecule present on a microarray of the present invention, or a transcription factor that binds such a nucleic acid molecule. Furthermore, Applicants have disclosed, and it is well understood in the art, that one use of the claimed microarrays is to determine relative binding efficiency of bound molecules. *See* the incorporated U.S. Patent No. 5,445,934 at column 22, lines 46-61. The Examiner denigrates that utility by asserting that hybridization to a molecule (such as the nucleic acid molecules on a claimed microarray) is not "a specific benefit, or an immediately applicable benefit". Final Action at page 5. Furthermore, such information determined from the use of the claimed microarrays provides a recognized and valuable benefit to practitioners in the art. The use of the claimed microarrays to efficiently and effectively provide a multitude of information based on the ability to isolate and identify nucleic acid molecules in a sample that are complementary to any of the nucleic acid molecules present on a claimed microarray, as well as identifying other biological molecules in a sample, is in itself useful.

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[5] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Applicants to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed microarrays.

In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other microarrays can be used for the same purpose, *i.e.*, binding other molecules. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not "specific" to the claimed microarray. The claimed microarrays, for example, comprise a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from the Markush group provided. *See, e.g.*, claim 8. The nucleic acid molecules of the claimed microarray are isolated, for example, from various samples derived from *Zea mays* such as ear tissue, kernel tissue, mature pollen, etc. *See* specification, at page 91, line 5 through page 99, line 7 (Example 1). A random microarray does not provide an equally good starting point to analyze large amounts of nucleotides which are complementary to any of the nucleotides of the claimed microarrays.[6] Moreover, the claimed microarrays allow one of ordinary skill in the art to design or customize a particular microarray tailored to the specific requirements of the artisan himself. *See, e.g.*, Petition under 37 C.F.R. § 1.144, filed January 10, 2003, at pages 7-10. Furthermore, even if a random microarray provided

[6] In the present case, unity of the nucleic acid sequences present in the claimed microarrays exists, for example, by virtue of their common utility as gene-specific hybridization targets to quantitatively measure expression of corresponding plant genes in *Zea mays*.

a better starting point for analysis than the claimed microarrays, it would not obviate the utility of the claimed microarrays. An invention may be "less effective than existing devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed microarrays could not be so used. Accordingly, the assertion of this utility as a probe for a multitude of nucleic acid molecules or as a means to assay relative binding efficiency of various nucleic acid molecules satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(2) The Claimed Microarrays Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also appears to assert that the disclosed uses are legally insufficient because they are not "substantial" utilities. Final Action at pages 3-6. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). " 'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[7]

There can be no question that one skilled in the art can use the claimed microarrays in a manner which provides an immediate benefit to the public, for example, to detect a mutation affecting the concentration of an mRNA or the pattern of expression encoded by one or more of the nucleic acid molecules present on a claimed microarray. The detection of such a mutation or

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[7] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

mutations provides an immediate benefit to the public because, *e.g.*, it enables a plant breeder to determine the potential of the expression response affecting a particular trait based on the genetic material in the progeny of a cross. This information about a plant's genetic profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

Quite apart from the detection of a mutation such as those described above, or the detection of a particular mRNA itself, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to the claimed microarrays comprising nucleic acid molecules. The utility of efficiently analyzing nucleic acid molecules and the nucleic acid sequences themselves, *i.e.*, ESTs, is not merely an academic issue. The real world value of ESTs is self-evident from the growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs. Like fermentation processes involving bacteria, ESTs and nucleic acid molecules with EST sequences are "industrial product[s] used in an industrial process – a useful or technical art if there ever was one." *In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for microarrays containing ESTs are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Cf. Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) ("People rarely, if ever, appropriate useless inventions"). Quite simply, the commercial value of microarrays is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

(3) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in

which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.[8] A challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107 at 2100-40.

Applicants have explicitly identified specific and substantial utilities, not only in the specification, but also in Applicants' Response dated June 18, 2002, at pages 6-9. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed microarrays will not work for the disclosed utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, Applicants have satisfied the requirement to provide a credible utility.

In view of the above, Applicants contend that the claimed microarrays are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of claims 8-11 under 35 U.S.C. §101 is improper and should be reversed.

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[8] Examples of incredible utilities are given in MPEP § 2107 at page 2100-34, and include:

> an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

C. The Claimed Microarrays Are Enabled by the Specification

The enablement of the claimed microarrays has been challenged. Claims 8-11 were erroneously rejected as not enabled by the specification, because the claimed microarrays allegedly lack utility and therefore cannot be enabled. Final Action at pages 6-7. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

D. The Specification Provides an Adequate Written Description of the Claimed Invention

Despite the Examiner's admission that the SEQ ID Numbers of the Markush group (in claim 8) and the combination (of claim 11) meet the written description provision of 35 U.S.C. § 112, first paragraph (Office Action mailed March 18, 2002, at page 7), the adequacy of the written description has been challenged by the Examiner because the microarrays of claims 8-11 are allegedly "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Final Action at page 7. The bases for the Examiner's challenge is that (1) "the claims recite the use of second nucleic acids that **comprise** the SEQ ID numbers, reading on the use of second nucleic acids that would be a full-length cDNA," and (2) "the claims are drawn to a microarray comprising nucleic acid molecules that are complementary to the second nucleic acid molecules," and thus would read on a full-length cDNA sequence that

would hybridize to a second nucleic acid. Final Action at pages 7-8 (emphasis in original). In short, the Examiner argues that (1) one of skill in the art would allegedly conclude that Applicants were not in possession of the nucleic acid molecules encompassed by the present invention, and (2) the specification "provides insufficient written description to support the genus encompassed by the claim." Office Action mailed March 18, 2002, at page 8. These are not proper bases for a written description rejection of a "comprising" claim. If they were, every "comprising" claim ever written would be invalid for failing to describe every nuance of the claimed invention. Furthermore, the specification demonstrates to one skilled in the art that Applicants were in possession of the claimed microarrays comprising the claimed genera of nucleic acid molecules.

(1) The Specification Reflects Applicants' Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if not every nuance, then the written description has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. A person of ordinary skill in the art would, after reading the present specification, understand that Applicants had possession a microarray comprising nucleic acid sequences selected from the group consisting of SEQ ID NOs: 5776, 5781, 5782, 5783, 5785, 5787, 5800, 5804, 5815, 5818, etc., and their complements, and therefore, the claimed invention.

Applicants have provided the nucleotide sequences required by the claims, *e.g.*, SEQ ID 5776, 5781, 5782, 5783, 5785, 5787, 5800, 5804, 5815, 5818, etc., and have disclosed

microarrays comprising such sequences, and have thus established possession of the claimed invention. Moreover, the present application describes more than just microarrays including the nucleotide sequences required by the claims. For example, it describes vectors comprising the claimed nucleic acid molecules, (*see, e.g.,* specification at page 67, line 14 through page 74, line 11) as well as plants transformed by the nucleic acid molecules of the present invention (*see, e.g.,* specification at page 74, line 16 to page 82, line 24). Thus, the fact that the claims at issue are intended to cover microarrays comprising nucleic acid molecules that include the recited sequences joined with additional sequences, or complements of the recited sequences does not mean that Applicants were any less in possession of the nucleic acid molecules of the claimed microarrays.[9] It is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

The present application describes more than just the claimed microarrays and the nucleic acid sequences of the claimed microarrays. For example, it describes how to make the nucleotide sequences and the libraries from which they were originally purified (specification at page 33, line 6 through page 39, line 25, and Examples 1-2). In addition, one of ordinary skill in the art has the ability to make and use the claimed microarrays based on the disclosure of the present specification, as well as envision a nucleic acid molecule that is complementary to any of the nucleic acid molecules of the claimed microarrays. Furthermore, the addition of extra nucleotides or detectable labels to the sequences present on the claimed microarrays is readily

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[9] If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then it goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

envisioned by one of ordinary skill in the art upon reading the present specification,[10] in particular at page 17, lines 20-24 (describing sequences with labels to facilitate detection); at page 62, line 8 through page 63, line 2 (describing site-directed mutagenesis of nucleic acid molecules); and at page 86, line 22 to page 87, line 3 (citing references describing the construction, manipulation and isolation of macromolecules). Moreover, it is well established that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (CCPA. 1981)).

(2) Applicants Have Described the Claimed Invention

The Final Action asserts that (1) "the claims recite the use of second nucleic acids that **comprise** the SEQ ID numbers, reading on the use of second nucleic acids that would be a full-length cDNA," and (2) "the claims are drawn to a microarray comprising nucleic acid molecules that are complementary to the second nucleic acid molecules" Final Action at pages 7-8 (emphasis in original). The Examiner appears to assert that each nucleic acid molecule within a genus must be described by its complete structure. Office Action mailed March 18, 2002, at page 8. These assertions are totally unfounded. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Applicants have satisfied that test for written description.

The claimed microarrays comprise combinations or collections of several genera of nucleic acid molecules. Each genus of nucleic acid molecules is complementary to at least one particular enumerated nucleotide sequence, for example., SEQ ID NOs: 5776, 5781, 5782, 5783,

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[10] It is established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *E.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

5785, 5787, 5800, 5804, 5815, 5818, etc. Applicants have disclosed common structural features for each genus of nucleic acid molecules, for example, SEQ ID NO: 5776. The respective common structural feature (*i.e.*, the complement or complements to a nucleotide sequence or sequences recited in the present claims) is shared by every nucleic acid molecule which may be included in a claimed microarray comprising a particular nucleic acid molecule; and the nucleic acid sequence of that nucleic acid molecule distinguishes the members of that genus of nucleic acid molecules from non-members. For example, if a microarray comprising a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence of SEQ ID NO: 5782, then it is a member of the claimed genus of microarrays comprising a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence of SEQ ID NO: 5782. If a microarray does not comprise a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence of SEQ ID NO: 5782, then it is not a member of that claimed genus.[11] The presence of other nucleotides at either end of the recited sequence will not interfere with the recognition of a claimed microarray as such – it either contains the nucleotides of SEQ ID NO: 5782 or it does not. One skilled in the art would clearly know if a microarray comprises a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences

[11] The same argument applies with equal force to every genus of the nucleic acid molecules included in the claimed microarrays. For example, if a microarray comprises a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence of SEQ ID NO: 5800, then it is a member of the genus of microarrays comprising a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence of SEQ ID NO: 5800.

and at least about 250 nucleotide residues and complementary to a molecule comprising any one or more of the recited nucleotide sequences. The fact that a nucleic acid molecule may comprise additional sequences, variations, or a full-length cDNA is beside the point. Such modifications are readily envisioned by one of ordinary skill in the art and disclosed throughout the specification.

In sum, because the specification demonstrates that Applicants had possession of the claimed invention, and have provided an adequate description of the claimed genera of microarrays comprising nucleic acid molecules that are complementary to a nucleic acid molecule comprising one of the recited SEQ ID NOs, the specification satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, and the rejection of claims 8-11 is improper and should be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,

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APPENDIX A

8. A microarray comprising a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from the group consisting of SEQ ID NO: 5776, SEQ ID NO: 5781, SEQ ID NO: 5782, SEQ ID NO: 5783, SEQ ID NO: 5785, SEQ ID NO: 5787, SEQ ID NO: 5800, SEQ ID NO: 5804, SEQ ID NO: 5815, SEQ ID NO: 5818, SEQ ID NO: 5821, SEQ ID NO: 5823, SEQ ID NO: 5828, SEQ ID NO: 5830, SEQ ID NO: 5832, SEQ ID NO: 5836, SEQ ID NO: 5838, SEQ ID NO: 5840, SEQ ID NO: 5845, SEQ ID NO: 5849, SEQ ID NO: 5850, SEQ ID NO: 5851, SEQ ID NO: 5856, SEQ ID NO: 5859, SEQ ID NO: 5863, SEQ ID NO: 5868, SEQ ID NO: 5871, SEQ ID NO: 5874, SEQ ID NO: 5875, SEQ ID NO: 5877, SEQ ID NO: 5893, SEQ ID NO: 5896, SEQ ID NO: 5901, SEQ ID NO: 5908, SEQ ID NO: 5909, SEQ ID NO: 5920, SEQ ID NO: 5922, SEQ ID NO: 5926, SEQ ID NO: 5928, SEQ ID NO: 5929, SEQ ID NO: 5931, SEQ ID NO: 5936, SEQ ID NO: 5937, SEQ ID NO: 5939, SEQ ID NO: 5941, SEQ ID NO: 5944, SEQ ID NO: 5945, SEQ ID NO: 5950, SEQ ID NO: 5955, SEQ ID NO: 5960, SEQ ID NO: 5961, SEQ ID NO: 5963, SEQ ID NO: 5964, SEQ ID NO: 5968, SEQ ID NO: 5973, SEQ ID NO: 5974, SEQ ID NO: 5991, SEQ ID NO: 5994, SEQ ID NO: 5999, SEQ ID NO: 6000, SEQ ID NO: 6001, SEQ ID NO: 6005, SEQ ID NO: 6006, SEQ ID NO: 6007, SEQ ID NO: 6011, SEQ ID NO: 6017, SEQ ID NO: 6018, SEQ ID NO: 6022, SEQ ID NO: 6023, SEQ ID NO: 6026, SEQ ID NO: 6030, SEQ ID NO: 6033, SEQ ID NO: 6042, SEQ ID NO: 6046, SEQ ID NO: 6059, SEQ ID NO: 6063, SEQ ID NO: 6065, SEQ ID NO: 6066, SEQ ID NO: 6089, SEQ ID NO: 6091, SEQ ID NO: 6098, SEQ ID NO: 6106, SEQ ID NO: 6107, SEQ ID NO: 6110, SEQ ID NO: 6117, SEQ ID NO: 6121, SEQ ID NO: 6124, SEQ ID NO: 6131, SEQ ID NO: 6137, SEQ ID NO: 6141, SEQ ID NO: 6144, SEQ ID NO: 6145, SEQ ID NO: 6147, SEQ ID NO: 6154, SEQ ID NO: 6167, SEQ ID NO: 6168, SEQ ID NO: 6170, SEQ ID NO: 6173, SEQ ID NO: 6178, and SEQ ID NO: 6181.

9. A microarray according to claim 8 where at least 75% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from said group.

10. A microarray according to claim 8 where at least 95% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from said group.

11. A microarray comprising nucleic acid molecules that are comprised of different sequences and at least about 250 nucleotide residues, wherein said nucleic acid molecules comprise nucleic acid sequences complementary to SEQ ID NO: 5776, SEQ ID NO: 5781, SEQ ID NO: 5782, SEQ ID NO: 5783, SEQ ID NO: 5785, SEQ ID NO: 5787, SEQ ID NO: 5800, SEQ ID NO: 5804, SEQ ID NO: 5815, SEQ ID NO: 5818, SEQ ID NO: 5821, SEQ ID NO: 5823, SEQ ID NO: 5828, SEQ ID NO: 5830, SEQ ID NO: 5832, SEQ ID NO: 5836, SEQ ID NO: 5838, SEQ ID NO: 5840, SEQ ID NO: 5845, SEQ ID NO: 5849, SEQ ID NO: 5850, SEQ ID NO: 5851, SEQ ID NO: 5856, SEQ ID NO: 5859, SEQ ID NO: 5863, SEQ ID NO: 5868, SEQ ID NO: 5871, SEQ ID NO: 5874, SEQ ID NO: 5875, SEQ ID NO: 5877, SEQ ID NO: 5893, SEQ ID NO: 5896, SEQ ID NO: 5901, SEQ ID NO: 5908, SEQ ID NO: 5909, SEQ ID NO: 5920, SEQ ID NO: 5922, SEQ ID NO: 5926, SEQ ID NO: 5928, SEQ ID NO: 5929, SEQ ID NO: 5931, SEQ ID NO: 5936, SEQ ID NO: 5937, SEQ ID NO: 5939, SEQ ID NO: 5941, SEQ ID NO: 5944, SEQ ID NO: 5945, SEQ ID NO: 5950, SEQ ID NO: 5955, SEQ ID NO: 5960, SEQ ID NO: 5961, SEQ ID NO: 5963, SEQ ID NO: 5964, SEQ ID NO: 5968, SEQ ID NO: 5973, SEQ ID NO: 5974, SEQ ID NO: 5991, SEQ ID NO: 5994, SEQ ID NO: 5999, SEQ ID NO: 6000, SEQ ID NO: 6001, SEQ ID NO: 6005, SEQ ID NO: 6006, SEQ ID NO: 6007, SEQ ID NO: 6011, SEQ ID NO: 6017, SEQ ID NO: 6018, SEQ ID NO: 6022, SEQ ID NO: 6023, SEQ ID NO: 6026, SEQ ID NO: 6030, SEQ ID NO: 6033, SEQ ID NO: 6042, SEQ ID NO: 6046, SEQ ID NO: 6059, SEQ ID NO: 6063, SEQ ID NO: 6065, SEQ ID NO: 6066, SEQ ID NO: 6089, SEQ ID NO: 6091, SEQ ID NO: 6098, SEQ ID NO: 6106, SEQ ID NO: 6107, SEQ ID NO: 6110, SEQ ID NO: 6117, SEQ ID NO: 6121, SEQ ID NO: 6124, SEQ ID NO: 6131, SEQ ID NO: 6137, SEQ ID NO: 6141, SEQ ID NO: 6144, SEQ ID NO: 6145, SEQ ID

NO: 6147, SEQ ID NO: 6154, SEQ ID NO: 6167, SEQ ID NO: 6168, SEQ ID NO: 6170, SEQ ID NO: 6173, SEQ ID NO: 6178, and SEQ ID NO: 6181.